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Optimizing Identification of Allergic Sensitization to Seasonal Inhalant Allergens in the USA: Implications for Constructing Optimal Panels to Evaluate Patients with Allergy

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Abstract

Introduction: While a specific number and type of antigens are recognized to detect perennial inhalant allergies, the optimal number and combination of allergens to reliably identify seasonal allergic sensitization is unclear due to limited national data. This study analyzed aeroallergen testing data from a large US clinical reference laboratory to provide guidance for optimizing seasonal allergen test selection. ***Methods:*** The 2019 serum IgE tests for seasonal inhalant allergens were identified from the Quest Diagnostics database. Patients with results for at least 1 of 31 seasonal allergens across 4 allergen classes (11 trees, 7 weeds, 5 grasses, and 8 molds) were analyzed. A step-by-step conditional approach was employed to determine the minimum number and species of allergens needed to identify at least 98% of sensitized patients for each class. ***Results:*** Of 88,042 patients tested for ≥1 seasonal allergen, 1.5%, 1.8%, 1.3%, and 1.6% were tested for all trees, weeds, grasses, and molds, respectively. Of those tested for all allergens within a class, 40.4%, 38.6%, 29.5%, and 21.2% were sensitized to at least one tree, weed, grass, or mold allergen, respectively. Identification of ≥98% of sensitized patients within a class required 8 allergens for trees (mountain cedar, maple box elder, walnut, white ash, elm, birch, cottonwood, and hickory/pecan), 5 for weeds (common ragweed short, rough pigweed, English plantain, lamb's quarters/goosefoot, and Russian thistle), 3 for grasses (June/Kentucky blue grass, Johnson grass, and Bermuda grass), and 7 for molds (*Alternaria alternata, Aspergillus fumigatus, Mucor racemosus, Epicoccum purpurascens, Penicillium notatum, Helminthosporium halodes,* and *Fusarium moniliforme*). ***Conclusion:*** A minimum of 23 antigens is required to optimally detect sensitization to four classes of seasonal allergens (i.e., ≥98% identification). The addition of these allergens to unique perennial allergens (cat, dog, mouse, cockroach, and 2 dust mite species) results in a comprehensive elucidation of inhalant allergen sensitization. This knowledge provides a pivotal guide for clinical laboratories as they construct allergen panels to optimize diagnostic yield.

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Introduction

Allergic sensitization to seasonal inhalant allergens plays a central role in pathogenesis of allergic diseases such as allergic rhinitis, asthma, and atopic dermatitis [1]. In addition to mitigation of allergens as part of comprehensive management of allergic diseases, identification of atopy helps differentiate allergic diseases from non-atopic diseases, which have similar signs and symptoms but warrant different treatments (e.g., allergic rhinitis vs. upper respiratory infections) [2, 3]. Allergen immunotherapy and some biologic therapies (e.g., omalizumab) also require identification of allergic sensitization [4].

Detecting sensitizing allergens may be accomplished via skin prick (SPT) or serum IgE (sIgE) testing. SPT in the United States (US) is a procedure usually performed by allergy specialists, while sIgE tests are performed in clinical laboratories and were once ordered by most providers [5, 6].

Currently, no large studies examine the minimal number of allergens required for detecting allergic sensitization toward seasonal allergens (tree, grass, weed, and mold) in the US. The American Academy of Asthma, Allergy, and Immunology (AAAAI) practice parameters on allergy diagnostic testing recommends that, in the US, up to 70 allergens may be tested utilizing epi-cutaneous skin or sIgE testing [5]. AAAAI reviewers found that on average 40 allergens were used for allergy testing among the US allergists [7].

Depending on local fauna and fauna, testing for many allergens may be needed to guide prescription of allergen extracts in allergen immunotherapy. However, fewer allergens may suffice to determine general allergic sensitization to trees, grasses, weeds, or molds. In this study, we determined the minimum number of allergens in each class required to identify the individuals sensitized to seasonal inhalant allergens based on data from sIgE tests.

Methods

In this cross-sectional, retrospective study, 88,042 patients were identified to have been tested for at least 1 of 31 seasonal allergens for four allergen classes (11 trees, 7 weeds, 5 grasses, and 8 mold allergens) in 2019 using sIgE testing at Quest Diagnostics, a national reference laboratory. All included aeroallergens were ordered individually, as opposed to by regional respiratory allergy panels, for the patients across the US who received testing for any cause. The focus on individually ordered aeroallergens aimed to mitigate the influence of arbitrary regional variations introduced by panel testing, thereby ensuring a more nationally representative dataset. Testing was performed using the ImmunoCAP™ specific IgE blood test that uses a fluoroenzyme immunoassay (non-RAST@) method. In this study, the threshold for a positive sIgE test, which was considered indicative of sensitization, was the level of detection (≥0.10 kU/L). This threshold was chosen instead of 0.35 kU/L for a positive test result based on recent recommendations suggesting that sIgE concentrations between 0.10 kU/L and 0.35 kU/L may be clinically relevant in some patients [8].

Four study populations were constructed, one for each aeroallergen class (tree, weed, grass, or mold), and each population comprises the patients who were tested for all individual allergens within the class. For a study population, or within a class, patients with at least one positive sIgE were considered atopic or sensitized for the class.

To determine the minimum number and species of allergens required to identify the sensitized patients for each class, a step-by-step conditional approach [9–13] was employed within each of the four-aeroallergen class. Essentially, the algorithm ranked the allergens from the one that yielded the highest increase in prevalence of sensitization to the one that gave the lowest, with the prevalence of sensitization for the whole population re-computed at each of the following steps:

1. Defined the most prevalent allergen in the whole population
2. Identified the next allergen that gave the highest increase in sensitization prevalence, in the subgroup of patients not sensitized to the previous allergen
3. Cycled through all allergens until none of the resulting ones induced a prevalence change
4. Determined the minimum number and species of allergens required to identify at least 98% of sensitized patients in a population, or within an aeroallergen class

Levels of urbanization categorized to describe the characteristics of sensitized patients were based on ERS' 2023 Rural-Urban Continuum Codes [14], a classification scheme that distinguishes metropolitan (metro) counties and nonmetropolitan (nonmetro) counties. The need for informed consent was waived as this study was deemed exempt by the WCG Institutional Review Board, an independent ethical review board, based on federal regulation 45 CFR Parts 46 and 164. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies [15]. Data analyses were performed using SAS Studio 3.6 on SAS version 9.4 (Cary, NC, USA).

Results

Of 88,042 patients (61.1% female, 37.9 [24.1] mean [SD] age) tested for ≥1 seasonal allergen in 2019, 1,281 (1.5%), 1,555 (1.8%), 1,149 (1.3%), and 1,394 (1.6%) were tested for all allergens within an aeroallergen class: 11 trees, 7 weeds, 5 grasses, and 8 molds, respectively. The demographic characteristics, census regional distribution, and levels of urbanization are reported for four study populations corresponding to four aeroallergen classes (Table 1). Compared to men, a higher proportion of women (63.0–64.8%) was observed consistently across all

Table 1. Characteristics of study populations

Characteristics	Tree (*n* = 1,281)	Weed (*n* = 1,555)	Grass (*n* = 1,149)	Mold (*n* = 1,394)
Age, years				
Mean±SD	41.9±22.7	47.4±21.1	39.8±23.4	44.8±22.4
Median	44.0	49.0	40.0	48.0
IQR (25th Pctl – 75th Pctl)	23.0–60.0	32.0–65.0	17.0–60.0	28.0–63.0
Age group, *n* (%)				
0–5 years	61 (4.8)	36 (2.3)	87 (7.6)	73 (5.2)
6–11 years	112 (8.7)	71 (4.6)	102 (8.9)	91 (6.5)
≥12 years	1,108 (86.5)	1,448 (93.1)	960 (83.6)	1,230 (88.2)
Gender, *n* (%)				
Female	822 (64.2)	1,008 (64.8)	724 (63.0)	894 (64.1)
Male	459 (35.8)	547 (35.2)	425 (37.0)	500 (35.9)
Census region, *n* (%)				
Northeast	165 (12.9)	200 (12.9)	167 (14.5)	157 (11.3)
Midwest	498 (38.9)	35 (2.3)	35 (3.1)	74 (5.3)
South	393 (30.7)	1,157 (74.4)	886 (77.1)	1,137 (81.6)
West	225 (17.6)	163 (10.5)	61 (5.3)	26 (1.9)
Metro level*, *n* (%)				
Big metro (population ≥1 million)	612 (47.8)	720 (46.3)	688 (59.9)	1,077 (77.3)
Small-to-medium metro (population <1 million)	570 (44.5)	656 (42.2)	380 (33.1)	224 (16.1)
Nonmetro	99 (7.7)	171 (11.0)	79 (6.9)	93 (6.7)
No data	0 (0.0)	8 (0.5)	2 (0.2)	0 (0.0)

*Classification derives from the Rural-Urban Continuum Codes (RUCC) published by the USDA Economic Research Service (2013).

aeroallergen classes. Of patients tested, the mean (SD) ages in years ranged from 39.8 (23.4) for grasses to 47.4 (21.1) for weeds. Of patients tested for trees, more were from the Midwest (38.9%) or the South (30.7%) than from the West (17.6%) or the Northeast (12.9%); of those tested for weeds, grasses, and molds, most were from the South (74.4–81.6%) and few were from the Midwest (2.3–5.3%) or the West (1.9–10.5%). Of patients tested for trees and weeds, slightly more were from big metro areas (population ≥1 million) than small-to-medium metro areas (trees: 47.8% vs. 44.5%; weeds: 46.3% vs. 42.2%), and the patients from nonmetro areas accounted for only 7.7% for trees and 11.0% for weeds. Of patients tested for grasses and molds, big-metro patients represented as high as 59.9% and 77.3%, respectively, while those from small-to-medium metro areas were 33.1% and 16.1%, followed by 6.9% and 6.7% nonmetro patients, respectively.

Of 1,281 patients tested for all 11 tree allergens, 517 (40.4%) were sensitized to at least one tree allergen (Table 2). By a step-by-step conditional approach, sensitization prevalence ranged from 26.3% when only the most prevalent allergen (mountain cedar) was tested to 40.4% when all 11 tree allergens were tested. Testing for 6 of 11 allergens (mountain cedar, maple box elder, walnut, white ash, elm, and birch) identified at least 95% of 517 sensitized patients; adding 2 more tree allergens (cottonwood, hickory/pecan) identified more than 98% of tree allergen-sensitized patients.

Of 1,555 patients tested for all 7 weed allergens, 600 (38.6%) were sensitized to at least one weed allergen (Table 2). By a step-by-step conditional approach, sensitization prevalence ranged from 30.6% when only the most prevalent allergen (common ragweed short) to 38.6% when all 7 weed allergens were tested. Testing for 4 of 7 allergens (common ragweed short, rough pigweed, English plantain, and lamb's quarters/goosefoot) identified at least 95% of 600 sensitized patients; adding one more weed allergen, Russian thistle, identified over 98% of weed-sensitized patients.

Of 1,149 patients tested for all 5 grass allergens, 339 (29.5%) were sensitized to at least one grass allergen (Table 2). By a step-by-step conditional approach, sensitization prevalence ranged from 26.5% when only the most prevalent grass (June/Kentucky blue) was tested to 29.5% when all 5 grass allergens were tested. Two of 5 allergens (June/Kentucky blue and Johnson) identified at

Table 2. Prevalence of sensitization, allergen ranked from the most prevalent to the one with the lowest increase in identifying additional sensitized patients

Class (*n*)	Ranking	Allergen	Prevalence, *n* (%)	Increase in identifying sensitized patients by adding allergen, *n* (%)
Tree (1,281)	1	Mountain cedar	337 (26.3)	
	2	Maple box elder	411 (32.1)	74 (5.8)
	3	Walnut tree	443 (34.6)	32 (2.5)
	4	White ash	467 (36.5)	24 (1.9)
	5	Elm	482 (37.6)	15 (1.1)
	6	Birch	494 (38.6)	12 (1.0)
	7	Cottonwood	504 (39.3)	10 (0.7)
	8	Hickory/pecan tree	**510 (39.8)**	**6 (0.5)**
	9	Sycamore	514 (40.1)	4 (0.3)
	10	Oak	517 (40.4)	3 (0.3)
	11	White mulberry	517 (40.4)	0 (0.0)
Weed (1,555)	1	Common ragweed short	476 (30.6)	
	2	Rough pigweed	537 (34.5)	61 (3.9)
	3	English plantain	563 (36.2)	26 (1.7)
	4	Lamb's quarters/ goosefoot	576 (37.0)	13 (0.8)
	5	Russian thistle	**587 (37.7)**	**11 (0.7)**
	6	Mugwort	595 (38.3)	8 (0.6)
	7	Sheep sorrel	600 (38.6)	5 (0.3)
Grass (1,149)	1	June grass Kentucky blue	305 (26.5)	
	2	Johnson grass	326 (28.4)	21 (1.9)
	3	Bermuda grass	**335 (29.2)**	**9 (0.8)**
	4	Timothy grass	338 (29.4)	3 (0.2)
	5	Bahia grass	339 (29.5)	1 (0.1)
Mold (1,394)	1	*Alternaria alternata*	190 (13.6)	
	2	*Aspergillus fumigatus*	223 (16.0)	33 (2.4)
	3	*Mucor racemosus*	249 (17.9)	26 (1.9)
	4	*Epicoccum purpurascens*	262 (18.8)	13 (0.9)
	5	*Penicillium notatum*	275 (19.7)	13 (0.9)
	6	*Helminthosporium halodes*	284 (20.4)	9 (0.7)
	7	*Fusarium moniliforme*	**291 (20.9)**	**7 (0.5)**
	8	*Cladosporium herbarum*	295 (21.2)	4 (0.3)

Bold: at least 98% of sensitized subjects are identified. Positive test defined as specific IgE ≥0.10 kU/L.

least 95% of 339 sensitized patients; adding Bermuda grass allergen identified more than 98% of sensitized grass allergen patients.

Lastly, of 1,394 patients tested for all 8 mold allergens, 295 (21.2%) were sensitized to at least one mold allergen (Table 2). By a step-by-step conditional approach, sensitization prevalence ranged from 13.6% when only the most prevalent one (*Alternaria alternata*) was tested to 21.2% when all 8 mold allergens were tested. Six of 8 allergens (*A. alternata, Aspergillus fumigatus, Mucor racemosus, Epicoccum purpurascens, Penicillium notatum,* and *Helminthosporium halodes*) identified at least 95% of 295 sensitized patients; adding one additional mold, *Fusarium moniliforme*, identified over 98% of mold sensitized patients. Overall, across all four seasonal aeroallergen classes combined, identifying ≥98% of sensitized patients required a minimum of 23 aeroallergens, including 8 allergens for trees, 5 for weeds, 3 for grasses, and 7 for molds. For the above 23 individual aeroallergens selected for identifying over 98% of sensitized patients by the conditional approach, the prevalence of sensitization based on testing one individual allergen at a time was calculated within class, for females and males, respectively (shown in Fig. 1).

Overall, males had a higher prevalence of sensitization than females in all individual allergens, across all four

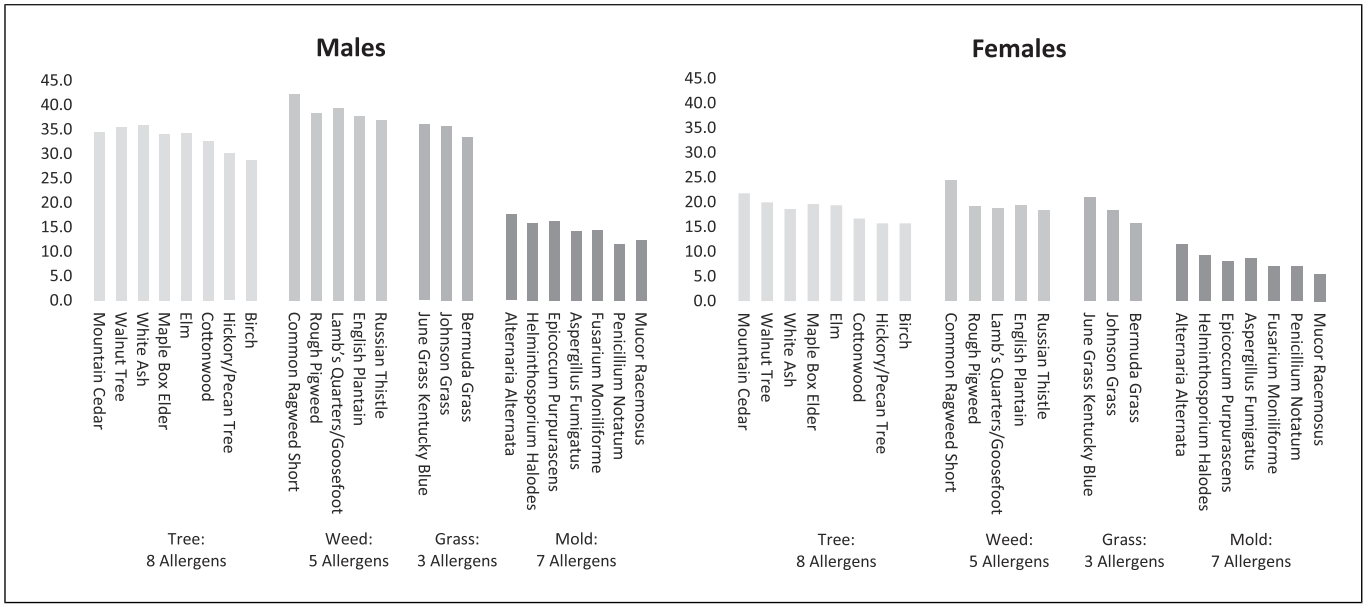

Fig. 1. Prevalence of sensitization for 23 selected individual seasonal allergens (sIgE ≥0.10 kU/L), by allergen class.

classes (shown in Fig. 1). For trees, males' prevalence of sensitization ranged from 30.6% (white ash) to 28.8% (birch) and females from 21.8% (mountain cedar) to 15.7% (birch and hickory/pecan). For weeds, males' prevalence ranged from 42.2% (common ragweed) to 36.9% (Russian thistle) and females from 24.3% (common ragweed) to 18.4% (Russian thistle). For grasses, males' prevalence ranged from 36.0% (June/Kentucky blue) to 33.4% (Bermuda grass) and females from 21.0% (June/Kentucky blue) to 15.8% (Bermuda). For molds, males' prevalence ranged from 17.6% (*A. alternata*) to 11.6% (*P. notatum*) and females from 11.4% (*A. alternata*) to 5.5% (*M. racemosus*).

Discussion

Testing for numerous antigens to determine seasonal inhalant allergen sensitization in allergic patients is both impractical and costly. Using too few tests may result in incomplete detection. Based on data from a national reference laboratory, this study demonstrates that a minimum of 23 antigens can successfully detect most patients sensitized to seasonal inhalant allergens. More specifically, a unique combination of 8 tree, 7 mold, 5 weed, and 3 grass species can detect sensitization in over 98% of sensitized patients. To the best of the authors' knowledge, this is the first study to investigate the optimal number of seasonal inhalant allergens for sIgE testing in the US.

The highest number of unique species required to identify sensitization was found in trees, followed by molds, weeds, and grasses. Because many grass species exhibit cross-reactivity, only 3 species were necessary to detect over 98% of those sensitized. Trees and weeds, on the other hand, rarely show cross-reactivity, thus necessitating a wider range of species for detection. There is no general cross-reactivity among the tree and weed species that we found necessary to detect 98% sensitization in this study. It remains unclear why multiple fungal species were needed to detect sensitization, as some evidence suggests common antigens and likely cross-reactivity among many fungal species [16, 17]. The significantly larger number of fungal species compared to trees, grasses, and weeds, higher atmospheric density of molds relative to other allergens, and geographic variations in prevalence may explain the need for multiple species to adequately detect mold-allergic patients [18].

Previous studies primarily reported the optimal number of allergens required to detect allergic sensitization outside the US. Most of these studies, however, were designed to detect sensitization to any inhalant allergen or the general state of atopy, which encompasses allergic sensitization to inhalants or foods. Therefore, fewer allergens were typically required. Two Chinese studies conducted in different geographic locations found that 8 seasonal and perennial allergens were needed to detect sensitization in most patients

with allergic rhinitis [9, 10]. Hu et al. [19] further demonstrated that 90% of sensitized patients with upper and lower respiratory tract allergic diseases could be detected by testing for dust mite, milk, cockroach, and *Alternaria* fungi antigens. In a South Korean cohort of allergic rhinitis patients, 5–7 inhalant allergens were required to detect most sensitized individuals [11]. Lastly, the World Allergy Organization (WAO) recommends the use of a combination of 18 inhalant and perennial allergens to detect allergic sensitization [12]. There was significant difference in tree allergens recommended by the WAO compared to ones in our study. Only birch and maple (plane) tree allergens were common between the two studies. This likely reflects differences in prevalence of tree allergen sensitization between Europe and North America. There were less of a difference between mold and weed allergens and since the WAO study used a grass mix for testing, we could not compare these pollens between the two studies.

In contrast to previous investigations, the present study aimed to detect sensitization to each of the four categories of seasonal allergens: trees, grasses, molds, and weeds. Using a broader panel of allergen tests beyond the minimum required for atopy diagnosis aligns with the recommendations of AAAAI. These guidelines advocate for the consistent use of evidence-based allergen panels in both clinical practice and research. Identifying additional sensitizing allergens within diverse seasonal categories expands the therapeutic options available for allergic patients [5]. For example, assessing atopy using a limited set of allergens can identify patients likely to benefit from antihistamines and intranasal corticosteroids. However, a deeper understanding of sensitization to specific seasonal allergen categories enables more targeted mitigation strategies. For instance, asthmatic patients with grass pollen and fungi sensitization may be at risk for severe exacerbations during thunderstorms that break these allergens into smaller respirable particles, resulting in deep pulmonary penetration [20, 21]. Such sensitized patients would benefit from allergen mitigation strategies during storms.

Identifying distinct sensitization to trees, grasses, weeds, or molds allows for the prescription of allergen immunotherapy, a highly effective approach for managing and potentially curing allergic rhinitis and asthma. There are theoretical advantages and disadvantages to using limited panels of allergens in designing allergen immunotherapy. The most logical disadvantage is that sensitizing allergens may be missed when using a small panel, especially among pollens with low cross-reactivity, such as trees and weeds. However, recent studies demonstrate efficacy even when only a limited number of sensitizing pollens are used because therapy with these is sufficient to induce T-regulatory cells that dampen allergic pathways [16, 22]. Conversely, among patients not sensitized to an allergen category, many allergens are not required to identify these patients, reducing the cost of testing with minimal loss of benefit. Arguably, using a limited number of allergens in the design of immunotherapy may be the optimal clinical and cost-effective strategy. Identifying a category of sensitizing allergens allows clinicians to test for other allergens in the same category if needed while reducing unnecessary testing to rule out categories of allergens for which patients are not allergic.

Most studies that determined the optimal panel size used SPT, not sIgE testing. There are differences between these two approaches; while SPT often uses the whole allergen, sIgE tests may focus on specific epitopes of the same allergen for in vitro assays. This may result in slightly different sensitivity and/or specificity between the two testing methods. Nonetheless, either SPT or sIgE tests are generally accepted in the US for managing respiratory allergies (such as allergic rhinitis and asthma), food allergies, and atopic dermatitis [5, 6]. Resolved component in vitro testing can enhance the specificity of allergen sensitization and characterize different phenotypes of allergic disease, such as predicting systemic reactions versus oral allergy syndrome with peanut ingestion by examining peanut components. Wider use of component testing may further optimize the allergen panel size [23, 24].

This study did not examine sensitization to perennial allergens, mostly indoor (e.g., dust mites, cats, dogs, cockroaches, and rodents), that also play a role in the pathogenesis of allergic disease [25, 26]. Including these allergens in a panel of 23 seasonal allergens we identified in this study creates a comprehensive "minimum ground floor" respiratory inhalant panel for managing respiratory allergic diseases in the US. This will enable healthcare providers to prescribe anti-allergy and anti-inflammatory therapies, implement targeted mitigation strategies, and offer allergen immunotherapy. Such a comprehensive panel would encompass no fewer than 29 allergens, including the 23 seasonal allergens defined by this study (i.e., 8 tree, 7 mold, 5 weed, and 3 grass), and 6 perennial allergens (1 cat, 1 dog, 1 cockroach, 2 dust mite, and 1 mouse species).

There are some limitations to our findings. First, unlike other investigations that exclusively tested patients with established allergic diseases, we did not ascertain the disease states of our cohorts, potentially including non-allergic

individuals in the analysis. Nevertheless, it is unlikely providers would order allergy tests without a strong suspicion of allergic pathology. Second, our data were collected from patients across the entire US, where there is a significant variation in regional flora. Therefore, our specific panel of seasonal allergens may not accurately detect all sensitizations in certain local areas with significantly different pollen distributions. This is potentially reflected in testing bias as there were significantly more tests performed in metro compared to non-metro regions (Table 1). Larger studies must be conducted to address this limitation. Third, we did not stratify sensitization by age. The prevalence of allergic sensitization varies from early childhood to early adulthood and then decreases toward senescence, potentially necessitating different minimum allergen numbers for detection in various age-groups [27, 28]. Younger patients were tested significantly less in our cohort, likely reflecting provider knowledge of these phenomena. Fourth, as mentioned previously, we used sIgE testing, while other studies used SPT. AAAAI recommends SPT as the first-line approach due to its good sensitivity and specificity, along with low per-unit costs for allergens and reagents [5]. However, most modern sIgE tests have similar diagnostic accuracy with comparable overall total costs [6]. Finally, the relatively small sample size of this study may not reflect true prevalence across the US. Nationally, regional sIgE panels are usually ordered when patients are tested for seasonal inhalant allergy; therefore, comprehensive testing of all seasonal allergens are relatively rare among patients. More importantly, to optimize identifying all potential seasonal allergens, including those not currently covered by regional panels – a primary emphasis of this study – we exclusively considered aeroallergens individually ordered, as opposed to those ordered through panels. Larger US studies using more allergens will support findings of the current study.

For optimal detection of allergic sensitization to seasonal allergens (i.e., ≥98% identification), at least 23 antigens are necessary. Testing with a minimum panel of 29 specific allergens, including the 23 seasonal allergens from this study and 6 additional perennial allergens, identifies most patients sensitized to distinct categories of inhalant seasonal and perennial allergens in the US. This information should be useful to clinical laboratories as they build allergen panels to optimize the diagnostic yield.

Statement of Ethics

This study protocol was reviewed and the need for approval was waived (deemed exempt) by the WCG Institutional Review Board based on federal regulation 45 CFR Parts 46 and 164. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies.

The need for informed consent was waived (deemed exempt) by the WCG Institutional Review Board based on federal regulation 45 CFR Parts 46 and 164. Informed consent was not obtained because the data used in the study were already de-identified and presented as aggregate data.

Conflict of Interest Statement

L.H.H. and Z.C. are employees of Quest Diagnostics and may own its stocks. L.S. declares no conflicts of interest. K.Y.K. is consultant and independent contractor for Thermo-Fisher Scientific.

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Author Contributions

K.Y.K., L.H.H., Z.C., and L.S. were involved in study and writing of manuscript. L.H.H. and Z.C. were involved in acquisition of study data. Z.C. was involved in data analysis.

Data Availability Statement

Data for this study are sole property of Quest Diagnostics and are not publicly available. Further inquiries can be directed to the corresponding author.

References

1 O'Hehir R, Holgate S, Sheikh A, Middleton E. Chapter 4. Middleton's allergy essentials. essay: Elsevier; 2017.

2 Meltzer EO, Blaiss MS, Derebery MJ, Mahr TA, Gordon BR, Sheth KK, et al. Burden of allergic rhinitis: results from the pediatric allergies in America survey. J Allergy Clin Immunol. 2009;124(3 Suppl l):S43–S70. https://doi.org/10.1016/j.jaci.2009.05.013.

3 Scadding GK, Kariyawasam HH, Scadding G, Mirakian R, Buckley RJ, Dixon T, et al. BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007). Clin Exp Allergy. 2017;47(7):856–89. https://doi.org/10.1111/cea.12953.

4 Normansell R, Walker S, Milan SJ, Walters EH, Nair P, Walker S. Omalizumab for asthma in adults and children. Cochrane Database Syst Rev. 2014;2014(1):CD003559. https://doi.org/10.1002/14651858.CD003559.pub4.
5 Bernstein IL, Li JT, Bernstein DI, Hamilton R, Spector SL, Tan R, et al. Allergy diagnostic testing: an updated practice parameter. Ann Allergy Asthma Immunol. 2008;100(3 Suppl 3):S1–148. https://doi.org/10.1016/s1081-1206(10)60305-5.
6 Hamilton RG. Clinical laboratory assessment of immediate-type hypersensitivity. J Allergy Clin Immunol. 2010;125(2 Suppl 2):S284–96. https://doi.org/10.1016/j.jaci.2009.09.055.
7 Cox L, Williams B, Sicherer S, Oppenheimer J, Sher L, Hamilton R, et al. Pearls and pitfalls of allergy diagnostic testing: report from the American college of allergy, asthma and Immunology/American Academy of allergy, asthma and Immunology specific IgE test task force. Ann Allergy Asthma Immunol. 2008;101(6):580–92. https://doi.org/10.1016/s1081-1206(10)60220-7.
8 Thorpe M, Movérare R, Fischer C, Lidholm J, Rudengren M, Borres MP. History and utility of specific IgE cutoff levels: what is the relevance for allergy diagnosis? J Allergy Clin Immunol Pract. 2023;S2213-2198(23):00560-3.
9 Lou H, Ma S, Zhao Y, Cao F, He F, Liu Z, et al. Sensitization patterns and minimum screening panels for aeroallergens in self-reported allergic rhinitis in China. Sci Rep. 2017;7(1):9286. https://doi.org/10.1038/s41598-017-10111-9.
10 Wang J, Wu Y, Li J, Huang X, Zhu R. Eight aeroallergen skin extracts may Be the optimal panel for allergic rhinitis patients in Central China. Int Arch Allergy Immunol. 2017;173(4):193–8. https://doi.org/10.1159/000479429.
11 Lee JE, Ahn JC, Han DH, Kim DY, Kim JW, Cho SH, et al. Variability of offending allergens of allergic rhinitis according to age: optimization of skin prick test allergens. Allergy Asthma Immunol Res. 2014;6(1):47–54. https://doi.org/10.4168/aair.2014.6.1.47.
12 Bousquet PJ, Burbach G, Heinzerling LM, Edenharter G, Bachert C, Bindslev-Jensen C, et al. GA2LEN skin test study III: minimum battery of test inhalent allergens needed in epidemiological studies in patients. Allergy. 2009;64(11):1656–62. https://doi.org/10.1111/j.1398-9995.2009.02169.x.
13 Sahiner UM, Civelek E, Yavuz ST, Büyüktiryaki AB, Tuncer A, Şekerel BE. Skin prick testing to aeroallergen extracts: what is the optimal panel in children and adolescents in Turkey? Int Arch Allergy Immunol. 2012;157(4):391–8. https://doi.org/10.1159/000329870.
14 USDA Economic Research Service. Rural urban Continuum Codes. 2013. Available from: https://www.ers.usda.gov/data-products/rural-urban-continuum-codes/documentation/#DataSources.
15 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344–9. https://doi.org/10.1016/j.jclinepi.2007.11.008.
16 Cox L, Nelson H, Lockey R, Calabria C, Chacko T, Finegold I, et al. Allergen immunotherapy: a practice parameter third update. J Allergy Clin Immunol. 2011;127(1 Suppl l):S1–55. https://doi.org/10.1016/j.jaci.2010.09.034.
17 Weber RW. Patterns of pollen cross-allergenicity. J Allergy Clin Immunol. 2003;112(2):229–40. https://doi.org/10.1067/mai.2003.1683.
18 Baxi SN, Portnoy JM, Larenas-Linnemann D, Phipatanakul W; Environmental Allergens Workgroup. Exposure and health effects of fungi on humans. J Allergy Clin Immunol Pract. 2016;4(3):396–404. https://doi.org/10.1016/j.jaip.2016.01.008.
19 Hu H, Huang H, Liao C, Li A, Zhang T, Liang X, et al. A study of allergen detection panel in Guangzhou, southern China based on real-world data from the past 7 years. Sci Rep. 2023;13(1):14855. https://doi.org/10.1038/s41598-023-41949-x.
20 D'Amato G, Liccardi G, Frenguelli G. Thunderstorm-asthma and pollen allergy. Allergy. 2007;62(1):11–6. https://doi.org/10.1111/j.1398-9995.2006.01271.x.
21 Pulimood TB, Corden JM, Bryden C, Sharples L, Nasser SM. Epidemic asthma and the role of the fungal mold Alternaria alternata. J Allergy Clin Immunol. 2007;120(3):610–7. https://doi.org/10.1016/j.jaci.2007.04.045.
22 Alvaro-Lozano M, Akdis CA, Akdis M, Alviani C, Angier E, Arasi S, et al. EAACI allergen immunotherapy user's guide. Pediatr Allergy Immunol. 2020;31(Suppl 25):1–101. https://doi.org/10.1111/pai.13189.
23 Hemmings O, Niazi U, Kwok M, Radulovic S, Du Toit G, Lack G, et al. Combining allergen components improves the accuracy of peanut allergy diagnosis. J Allergy Clin Immunol Pract. 2022;10(1):189–99. https://doi.org/10.1016/j.jaip.2021.08.029.
24 Dramburg S, Hilger C, Santos AF, de Las Vecillas L, Aalberse RC, Acevedo N, et al. EAACI molecular allergology user's guide 2.0. Pediatr Allergy Immunol. 2023;34(Suppl 28):e13854. https://doi.org/10.1111/pai.13854.
25 Wise SK, Lin SY, Toskala E, Orlandi RR, Akdis CA, Alt JA, et al. International consensus statement on allergy and rhinology: allergic rhinitis. Int Forum Allergy Rhinol. 2018;8(2):108–352. https://doi.org/10.1002/alr.22073.
26 Kuzdak M, Jerzynska J, Stelmach I, Podlecka D, Majak P, Janas A, et al. Associations between sensitization to perennial/seasonal allergens and childhood asthma. Allergol Select. 2018;2(1):151–5. https://doi.org/10.5414/ALX01882E.
27 Kwong K, Robinson M, Sullivan A, Letovsky S, Liu AH, Valcour A. Fungal allergen sensitization: prevalence, risk factors, and geographic variation in the United States. J Allergy Clin Immunol. 2023;152(6):1658–68. https://doi.org/10.1016/j.jaci.2023.09.010.
28 Salo PM, Arbes SJ Jr, Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. J Allergy Clin Immunol. 2014;134(2):350–9. https://doi.org/10.1016/j.jaci.2013.12.1071.